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EFFECT OF RENIN-ANGIOTENSIN SYSTEM INHIBITORS FOR RECURRENCE OF PAROXYSMAL ATRIAL FIBRILLATION DEPENDING ON A1166C POLYMORPHISM

Introduction. Atrial fibrillation (AF) is one of the most important medical and social problems in modern society, which is a common cause of ischemic stroke and leads to disability. The incidence of embolic complications is about 2.1% per year among patients with paroxysmal AF, and is currently considered a potentially dangerous arrhythmia with a significant increase in the incidence of serious complications (Hindricks G., 2020).

In recent years, the results of large multicenter clinical studies of cardio- and angioprotective properties of antihypertensive drugs have become widely available. The LIFE study (Losartan Intervention for End Point Reduction in Hypertension) found a lower risk of developing AF in patients with baseline systolic blood pressure (SBP) ≤130 mm Hg. (risk ratio 0.60; 95% CI 0.45-0.82) than in patients with SBP ≥141 mm Hg. (Okin P.M., 2015).

In their study, E. Takii et al. showed the effect of ARBs for the secondary prevention of AF paroxysms. The authors concluded that losartan suppressed the maximum duration and total duration of AF paroxysms in patients without hemodynamic changes (Takii E., 2016).

However, there is another view that the use of ACE inhibitors and ARBs is not justified in the secondary prevention of AF recurrence. At least, if there are no other indications for the use of these drugs (Disertori M., 2012).

Atrial fibrillation is a multifactorial disease, in the development of which such factors as old age, arterial hypertension and environment play an important role, as well as genetic predisposition. The risk of development increases in those who have a history of at least one parent with this arrhythmia. Up to a third of patients with this arrhythmia have common genetic variants that predispose to AF. Currently, it is especially important to study the role of the genes of the renin-angiotensin-aldosterone system (RAAS), since recent data confirm that it is precisely its activation that plays a leading role in the preservation of AF (Topal N.P.,2011; Tucker, N. R., 2016).

Such studies are of great practical interest for cardiologists, since the establishment of the relationship of genetic factors with the RAAS mediators and the inhibitors of the renin-angiotensin system will allow preventing the recurrence of arrhythmia in a particular patient. Therefore, in connection with the above, it is of interest to determine the relative risk of recurrence of paroxysmal atrial fibrillation with the use of renin-angiotensin system inhibitors, taking into account the A1166C polymorphism of the AGTR1 gene, which determined the purpose of this work.

The aim of the study. To determine effect of renin-angiotensin system inhibitors for recurrence of paroxysmal atrial fibrillation depending on A166C polymorphism.

Materials and methods. To achieve this goal, a prospective study was conducted on the basis of the Communal uncommercial company “City Hospital № 10” of Zaporizhzhia City Council. The sample of patients was conducted in the

period from 2014 to 2019. The results of the study are based on data from a comprehensive examination and dynamic monitoring of 92 patients with paroxysmal AF on the background of coronary heart disease with hypertension from the city of Zaporozhye. The observation period was 6 months.

Detection of gene polymorphism was made by polymerase chain reaction (PCR). Genomic DNA was isolated from peripheral blood leukocytes using a standard DNA express blood test system (Litech, Russia) according to the manufacturer's instructions. Determination of SNP (Single Nucleotide Polymorphism) of A1166C polymorphism in the angiotensin II receptor gene (AGTR1) gene was performed by real-time PCR using a Rotor-Gene 6000 amplifier (Corbett Research, Australia). The structure of primers from standard sets "SNP-express-RV" (Litech) was used.

Treatment of patients. Prescribed β-blocker - bisoprolol ("Bisoprolol-Ratiopharm", Ratiopharm) in an initial dose of 2.5 mg in the morning once a day, followed by dose titration to 5-10 mg depending on individual sensitivity to the drug. The average dose of the drug was (5.0 ± 0.2) mg. The anticoagulant rivaroxaban (Xarelto, Bayer) was prescribed to all patients at 20 mg once daily during meal time. Atorvastatin (Torvacard-Crystal, Sanofi) 20 mg once daily was also prescribed. To assess the effect of renin-angiotensin system inhibitors for recurrence of paroxysmal atrial fibrillation, patients were divided into 2 subgroups. Adaptive randomization was prescribed to 47 patients ACE inhibitor perindopril (Prestarium, Servier) 4 mg 1 time per day in the morning, before meals and 45 individuals angiotensin II receptor blocker losartan 50 mg 1 time per day (Lozap, Sanofi).

Obtained results. In the perindopril subgroup of 47 subjects, 15 patients had recurrence of arrhythmias and 32 had none, and in the losartan subgroup of 45 subjects, 9 patients had recurrence of arrhythmias and 36 had none. The relative risk of arrhythmia recurrence with losartan was 0.627, CI RR 0.306-1.285, but RR was inaccurate because 95% of CI RR crossed 1. There were 19 individuals in the perindopril subgroup with the A1166C allele C gene: 10 individuals with arrhythmia recurrence and 9 without. In the losartan subgroup of 18 subjects with the C allele

gene: 3 patients had arrhythmia recurrence and 15 had none. RR relative to arrhythmia recurrence was 0.317, CI RR 0.104-0.968.

Conclusions. Thus, when studying the effect of renin-angiotensin system inhibitors on the activity of the cardiovascular system, it is advisable to take into account the genetic characteristics of patients with paroxysmal AF. It was found that genetic polymorphism of A1166C may affect susceptibility to ACE inhibitors and ARBs. Combination therapy with the inclusion of losartan is significantly more effective in patients with allelic gene C polymorphism A1166C and reduces the risk of arrhythmia recurrence by 0.32, 95 CI RR 0,104-0,968.